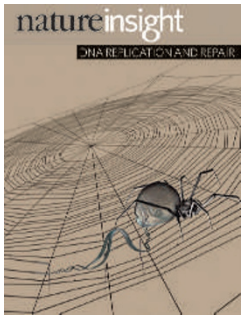

Cover illustration
The integrity of inheritance, like the strength of a spider web, is weakened by disruption or damage. (Courtesy of J. Young and A. Nussenzweig.)

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DNA REPLICATION AND REPAIR

In the beginning, there was nucleic acid. Evolutionary biologists have argued persuasively that nucleic acids were the original self-replicating entity, an idea encapsulated in the RNA-world hypothesis. And it remains true to this day that the genome is the fundamental component required for the existence of a cell or a virus.

Given this heavy responsibility for the maintenance of life, ensuring the integrity of the genome from one generation to the next (the occasional beneficial mutation notwithstanding) is crucial. There are two aspects to this process: accurate replication of the nucleic acid so that daughter cells inherit a complete genome, and reversal of any damage that might hinder replication or alter the encoded information.

The reviews in this Insight cover aspects of repair and replication that contribute to accurate propagation of genetic information. As we have learned in the past decade, these processes are highly interconnected.

We begin at the end — at the chromosome ends, or telomeres, where the cell uses special 'tricks' during replication, to prevent the shortening of chromosomes. In addition, the cell needs to ignore the similarity between the ends of the telomeres and double-strand breaks in DNA so that the telomere ends are not 'repaired' inappropriately. The genome can also be disrupted during replication of the rest of the chromosome, through increased instability of triplet repeats, and several mechanisms suppress this instability. In addition to such endogenous disruption, DNA can be damaged by factors such as oxygen radicals or ultraviolet radiation. DNA lesions caused by such exogenous factors need to be repaired so that they do not impede the replication machinery. Finally, in the larger context, cellular DNA is packaged in a proteinaceous sheath, so interesting questions arise about how the replication and repair complexes gain access to the DNA.

When replication goes awry or DNA lesions occur, ageing and disease can result. Studies in this field might help us to mitigate such outcomes in the future.

Angela K. Eggleston, Senior Editor

REVIEWS

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